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=> d ide can l5

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 1994 ACS
RN   83-74-9  REGISTRY
CN   Ibogamine, 12-methoxy- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine
     deriv. (9CI)
CN   Ibogaine (7CI, 8CI)
OTHER NAMES:
CN   (-)-Ibogaine
CN   Ibogain
FS   STEREOSEARCH
DR   17378-46-0
MF   C20 H26 N2 O
CI   COM
LC   STN Files:   ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD,
       CEN, CHEMLIST, CIN, CSCHEM, DDR, DRUGNL, DRUGR, DRUGU,
       DRUGUPDATES, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
       MRCK*, NAPRALERT, PNI, PROMT, SPECINFO, TOXLINE, TOXLIT
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DES  4:.IBOGAMINE

Absolute stereochemistry.
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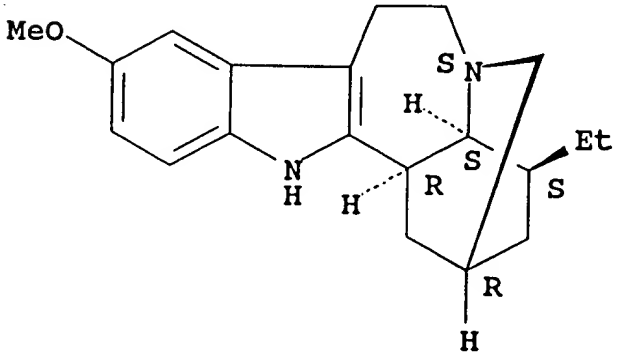

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L22          75 S L5 OR L18
L23       81529 S METABOLITE#
L24           8 S L22 AND L23

     FILE 'WPIDS' ENTERED AT 12:11:40 ON 14 OCT 94
L25           8 S L18
L26        1748 S METABOLITE#
L27           0 S L25 AND L26

     FILE 'HCA, HCAPREVIEWS, BIOSIS, EMBASE' ENTERED AT 12:12:37 ON 14
     OCT 94
L28          12 DUP REMOVE L14 L16 L24 L21 (15 DUPLICATES REMOVED)


=> fil hca hcaprev biosis embase
FILE 'HCA' ENTERED AT 12:13:22 ON 14 OCT 94
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=> d 1-12 l28 bib ab

L28  ANSWER 1 OF 12  BIOSIS  COPYRIGHT 1994 BIOSIS
AN   94:410600  BIOSIS
DN   97423600
TI   Evidence that ibogaine releases dopamine from the
     cytoplasmic pool in isolated mouse striatum.
AU   Harsing L G Jr; Sershen H; Lajtha A
CS   Cent. Neurochem., Nathan Kline Inst. Psychiatric Res., Orangeburg, NY
     10962, USA
SO   Journal of Neural Transmission General Section 96 (3). 1994.
     215-225.
LA   English
AB   We measured the effect of ibogaine on the tritium efflux
     from isolated mouse striatum preloaded with (3H)dopamine ((3H)DA).
     Ibogaine increased the basal tritium outflow in a
     concentration-dependent manner, but it was without effect on
     electrical stimulation-induced tritium overflow. Separation of the
     released radioactivity after ibogaine administration showed
     that this drug increased the release of (3H)DA and
     (3H)-dihydroxyphenylacetic acid ((3H)DOPAC), but the efflux of
     O-methylated-deaminated metabolites was not changed. The
     dopamine (DA)-releasing effect of ibogaine was reduced by
     the DA uptake inhibitors cocaine and nomifensine. The tritium efflux
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evoked by **ibogaine** was not altered by omission of Ca-2+ from the perfusion buffer or by inhibition of the voltage-sensitive Na+ channels with tetrodotoxin. Ibogaine maintained its effect on release from superfused striatum prepared from reserpine-pretreated mice. The **ibogaine**-induced tritium release measured from mouse striatum that was preloaded with (3H)DA was not affected by the D-2 DA receptor ligands (-)-quinpirole and (+/-)-sulpiride, indicating that the **ibogaine**-induced release is not subject to presynaptic autoreceptor regulation. Ibogaine failed to affect (3H) DA uptake and retention in mouse striatum. Thes data indicate that at the nerve terminal level **ibogaine** releases DA, and the primary source for the release is probably the cytoplasmic pool. The DA-releasing effect of **ibogaine** may have importance in mediation of its hallucinogenic action, as seen in a frequent practice in African cults.

L28 ANSWER 2 OF 12 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN 94206613 EMBASE
TI Evidence that **ibogaine** releases dopamine from the cytoplasmic pool in isolated mouse striatum.
AU Harsing L.G. Jr.; Sershen H.; Lajtha A.
CS Center for Neurochemistry, Nathan Kline Inst Psychiatric Res, Orangeburg, NY 10962, United States
SO J. NEURAL TRANSM. GEN. SECT., (1994) 96/3 (215-225).
ISSN: 0300-9564 CODEN: JNTMAH
CY Austria
DT Journal
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB We measured the effect of **ibogaine** on the tritium efflux from isolated mouse striatum preloaded with [3H]dopamine ([3H]DA). **Ibogaine** increased the basal tritium outflow in a concentration-dependent manner, but it was without effect on electrical stimulation-induced tritium overflow. Separation of the released radioactivity after **ibogaine** administration showed that this drug increased the release of [3H]DA and [3H]-dihydroxyphenylacetic acid ([3H]DOPAC), but the efflux of O-methylated-deaminated **metabolites** was not changed. The dopamine (DA)-releasing effect of **ibogaine** was reduced by the DA uptake inhibitors cocaine and nomifensine. The tritium efflux evoked by **ibogaine** was not altered by omission of Ca2+ from the perfusion buffer or by inhibition of the voltage-sensitive Na+ channels with tetrodotoxin. **Ibogaine** maintained its effect on release from superfused striatum prepared from reserpine-pretreated mice. The **ibogaine**-induced tritium release measured from mouse-striatum that was preloaded with [3H]DA was not affected by the D-2 DA receptor ligands (-)-quinpirole and (+/-)-sulpiride, indicating that the **ibogaine**-induced release is not subject to presynaptic autoreceptor regulation. **Ibogaine** failed to affect [3H]DA uptake and retention in mouse striatum. These data indicate that at the nerve terminal level

ibogaine releases DA, and the primary source for the rel ase is probably the cytoplasmic pool. The DA-releasing effect of **ibogaine** may have importance in mediation of its hallucinogenic action, as seen in a frequent practice in African cults.

L28 ANSWER 3 OF 12 CApreviews COPYRIGHT 1994 ACS DUPLICATE 1
AN 94:485878 CApreviews
TI Effects of iboga alkaloids on morphine and cocaine self-administration in rats: relationship to tremorigenic effects and to effects on dopamine release in nucleus accumbens and striatum
AU Glick, S. D.; Kuehne, M. E.; Raucci, J.; Wilson, T. E.; Larson, D.; Keller, R. W. Jr.; Carlson, J. N.
CS Department of Pharmacology and Toxicology (A-136), Albany Medical College and the Capital District Center for Drug Abuse Research and Treatment, Albany, NY, 12208, USA
SO Brain Res. (1994), 657(1-2), 14-22
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB **Ibogaine**, a naturally occurring alkaloid, has been claimed to be effective in treating addiction to opioid and stimulant drugs and has been reported to decrease morphine and cocaine self-administration in rats. The present study sought to det. if other iboga alkaloids, as well as the chem. related harmala alkaloid harmaline, would also reduce the i.v. self-administration of morphine and cocaine in rats. Because both **ibogaine** and harmaline induce tremors, an effect that may be causally related to neurotoxicity in the cerebellar vermis, the temorigenic activities of the other iboga alkaloids were assessed. Lastly, in view of the involvement of the dopaminergic mesolimbic system in the actions of drugs of abuse, the effects of some of the iboga alkaloids on extracellular levels of dopamine and its **metabolites** in the nucleus accumbens and striatum were detd. All of the tested alkaloids (i.e., **ibogaine**, tabernanthine, R- and S-coronaridine, R- and S-ibogamine, desethylcoronaridine, and harmaline) dose-dependently (2.5-80 mg/kg) decreased morphine and cocaine intake in the hour after treatment; decreases in morphine and cocaine intake intake were also apparent the day after administration of some but not all of these alkaloids (i.e., **ibogaine**, tabernanthine, desethylcoronaridine, and the R-isomers of coronaridine and ibogamine). In some rats, there were persistent decreases in morphine or cocaine intak for several days after a single injection or after two or three weekly injections of one or another of these alkaloids; R-ibogamine produced such effects more consistently than any of the other alkaloids. At the doses used to assess effects on drug self-administration, **ibogaine** , tabernanthine, desethylcoronaridine and harmaline all induced tremors for at least 2-3 h; both enantiomers of both coronaridine and ibogamine induced very weak or no tremors. Using in vivo microdialysis, the effects of the R- and S-enantiomers of coronaridine and ibogamine on extracellular dopamin levels in the nucleus accumbens and striatum were compared. The R-enantiomers decreased dopamine levels in both brain regions whereas the

S-enantiomers produced no significant changes in dopamine levels in either region. The results of this study indicate that the 'anti-addictive' and tremorigenic effects of the iboga alkaloids can be dissocd. and that long-term effects of these alkaloids n drug self-administration appear to be related to initial decreases in dopaminergic activity in specific brain areas.

L28 ANSWER 4 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 2
AN 119:262348 CA
TI Inhibitory effects of ibogaine on cocaine self-administration in rats
AU Cappendijk, Susanne L. T.; Dzoljic, Michailo R.
CS Fac. Med. Health Sci., Erasmus Univ. Rotterdam, Rotterdam, 3000 DR, Neth.
SO Eur. J. Pharmacol. (1993), 241(2-3), 261-5
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB In order to det. the potential antiaddictive properties of **ibogaine**, the cocaine self-administration model was used in rats. A single injection of **ibogaine** (40 mg/kg i.p.) produced a decrease of cocaine intake, which lasted for >48 h. Since the half-life time of **ibogaine** is short, this might suggest the involvement of one or several active **metabolites** of **ibogaine** in regulating cocaine intake. Repetitive administration of **ibogaine** on 3 consecutive days also induced a pronounced decrease of cocaine intake. However, a more prominent inhibitory effect on cocaine intake was obsd. in animals treated repeatedly with **ibogaine**, 40 mg/kg i.p. once each week for 3 consecutive weeks. These results indicate that **ibogaine** or its **metabolite**(s) is a long-lasting interruptor of cocaine dependence, which supports similar observations from uncontrolled clin. studies.

L28 ANSWER 5 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 3
AN 120:69440 CA
TI Local effects of **ibogaine** on extracellular levels of dopamine and its **metabolites** in nucleus accumbens and striatum: interactions with D-amphetamine
AU Glick, S. D.; Rossman, K.; Wang, S.; Dong, N.; Keller, R. W. Jr.
CS Department of Pharmacology and Toxicology (A-136), and the Capital District Center for Drug Abuse Research and Treatment, Albany Medical College, New Scotland Avenue, Albany, NY, 12208, USA
SO Brain Res. (1993), 628(1-2), 201-8
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Systemic administration of **ibogaine** (40 mg/kg, i.p.) has been reported to induce both acute (1-3 h) and persistent (19-20 h) changes in extracellular levels of dopamine and its **metabolites** in the nucleus accumbens and striatum. In the present study, local administration of **ibogaine** to the striatum and nucleus accumbens produced effects that mimicked both the acute and persistent effects of systemic administration:

perfusion with high concns. (200 and 400 .mu.M) of **ibogaine** mimicked the acute effects (decreased extracellular dopamine levels and increased extracellular **metabolite** levels) whereas perfusion with a low concn. (10 .mu.M) of **ibogaine** mimicked the persistent effects (decreased extracellular levels of DOPAC). These results indicate that **ibogaine** acts directly in brain regions contg. dopaminergic nerve terminals and that long-lasting effects of systemically administered **ibogaine** might be mediated by persisting low levels of **ibogaine**. Locally administered **ibogaine** (10 .mu.M) was also found to enhance the effects of systemically administered D-amphetamine (1.25 mg/kg, i.p.) on extracellular dopamine levels, and conversely, systemically administered **ibogaine** (40 mg/kg, i.p.; 19 h pretreatment) enhanced the effects of locally administered D-amphetamine (1-10 .mu.M). These results indicate that, in addn. to a metabolic mechanism implicated previously, a pharmacodynamic mechanism contribut s to the interaction between **ibogaine** and D-amphetamine. The relevance of such mechanisms to claims regarding **ibogaine** 's anti-addictive properties is unclear.

L28 ANSWER 6 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 4
AN 116:166169 CA
TI Ibogaine antagonizes cocaine-induced locomotor stimulation in mice
AU Sershen, Henry; Hashim, Audrey; Harsing, Laszlo; Lajtha, Abel
CS Div. Neurochem., Nathan S. Kline Inst., Orangeburg, NY, 10962, USA
SO Life Sci. (1992), 50(15), 1079-86
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB **Ibogaine** (40 mg/kg i.p.), when given 2 h before an acute injection of cocaine (25 mg/kg s.c.) to C57BL/6 mice, reduced the cocaine-induced locomotor stimulation. Such stimulation was also reduced in the **ibogaine**-treated mice when a second injection of cocaine was given 24 h later. Thus, the redn. in locomotor activity was not just the short-term depression of locomotor activity seen after **ibogaine** administration. When mice were given a daily injection of cocaine for 3 days and **ibogaine** was given after the cocaine injection on day 3, and again on day 4, cocaine-induced locomotor activity was reduced three hours later on day 4. On days 5 and 9 of the cocaine administration, with no further **ibogaine** treatment ambulatory counts were still lower in the **ibogaine** -pretreated mice. Locomotor stimulation induced by amphetamine (10 mg/kg) was not affected by **ibogaine**. An acute injection of **ibogaine** resulted in a transient increase in turnover of dopamine, as indicated by the increase in the ratio of **metabolites** of the dopamine to dopamine, followed by a decrease in the **metabolites** in striatum and frontal cortex 24 h later. In vivo treatment with **ibogaine** did not affect the binding of [3H]WIN 35,248 to the cocaine binding site in striatal tissue measured in vitro. In addn., **ibogaine** added in vitro had a weak affinity to the WIN 35,248 binding site (IC50 for cocaine = 120 nM and for **ibogaine** = 1,500 nM).

The results suggest that **ibogaine** may have induced a selective change in the dopaminergic system that results in a decrease in responsiveness to cocaine that persisted for at least 1 wk.

L28 ANSWER 7 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 5
AN 117:163813 CA
TI Ibogaine reduces amphetamine-induced locomotor stimulation in C57BL/6By mice, but stimulates locomotor activity in rats
AU Sershen, Henry; Harsing, Laszlo G., Jr.; Hashim, Audrey; Lajtha, Abel
CS Div. Neurochem., Nathan S. Kline Inst. Psychiatr. Res., Orangeburg, NY, 10962, USA
SO Life Sci. (1992), 51(13), 1003-11
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB The effect of **ibogaine** hydrochloride on locomotor stimulation induced by d-amphetamine sulfate was tested in male C57BL/6By mice and in female Sprague-Dawley rats. In mice, locomotor stimulation induced by d-amphetamine at 1 or 5 mg/kg s.c. was reduced by prior administration of one or two injections of **ibogaine** (40 mg/kg), given 2 or 18 h earlier. This redn. in locomotor activity persisted for two days. Locomotor stimulation induced by a higher dose (10 mg/kg) of d-amphetamine was not reduced by such prior administration of **ibogaine**. A lower dos of **ibogaine** (20 mg/kg) did not reduce the subsequent locomotor activity induced by d-amphetamine. **Ibogaine** decreased striatal dopamine levels, while d-amphetamine increased them. **Ibogaine** treatment (2 .times. 40 mg/kg, 18 h apart) induced a decrease by 30% in the level of striatal dopamin and its **metabolites** measured in tissue exts. 3 h after the second **ibogaine** injection. One hour after d-amphetamine (5 mg/kg) administration, the level of striatal dopamine increased by 26%. Although the level of striatal dopamine was initially lower in the **ibogaine**-pretreated mice, d-amphetamine (5 mg/kg) administration induced an increase in striatal dopamine and its **metabolites**. The effect of **ibogaine** seems to be species specific, since in rats pretreated with **ibogaine** 18 h before d-amphetamine, locomotor stimulation induced by d-amphetamine was further increased. In addn., the in vitro elec.-evoked release of [3H]dopamine from striatal tissue was either unchanged or inhibited in the presence of d-amphetamine, and after **ibogaine** pretreatment in vivo, the release of tritium in the presence of d-amphetamine was inhibited or stimulated in mice and rats, resp.

L28 ANSWER 8 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 6
AN 116:143736 CA
TI Mechanisms of action of ibogaine and harmaline congeners based on radioligand binding studies
AU Deecher, Darlene C.; Teitler, Milton; Soderlund, David M.; Bornmann, William G.; Kuehne, Martin; Glick, Stanley D.
CS Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA

SO Brain Res. (1992), 571(2), 242-7
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Assays using radioligands were used to assess the actions of **ibogaine** and harmaline on various receptor types. **Ibogaine** congeners showed affinity for opiate receptors whereas harmaline and harmine did not. The Ki for coronaridine was 2.0 .mu.M at .mu.-opiate receptors. The Kis for coronaridine and tabernanthine at the .delta.-opiate receptors were 8.1 and 3.1 .mu.M, resp. **Ibogaine**, ibogamine, coronaridine, and tabernanthine had Ki values of 2.08, 2.6, 4.3 and 0.15 .mu.M, resp., for .kappa.-opiate receptors. Long-lasting, dose-dependent behavioral effects of **ibogaine** have been reported. The possibility that these effects were due to irreversible binding properties of **ibogaine** at .kappa.-receptors was considered; however, radioligand wash expts. showed a rapid r covery of radioligand binding after one wash. A voltage-dependent sodium channel radioligand demonstrated Ki values in the .mu.M rang for all drugs tested. Using radioligand binding assays and/or 36Cl-uptake studies, no interaction of **ibogaine** or harmaline with the GABA receptor-ionophore was found. The .kappa.-activity of **ibogaine** (or an active **metabolite**) may be responsible for its putative anti-addictive properties whereas the tremorigenic properties of **ibogaine** and harmaline may be due to their effects on sodium channels.

✓L28 ANSWER 9 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 7
AN 116:248274 CA
TI Acute and prolonged effects of ibogaine on brain dopamine metabolism and morphine-induced locomotor activity in rats
AU Maisonneuve, I. M.; Rossman, K. L.; Keller, R. W., Jr.; Glick, S. D.
CS Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA
SO Brain Res. (1992), 575(1), 69-73
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB **Ibogaine**, an indoalkylamine, proposed for use in treating opiate and stimulant addiction, has been shown to modulate the dopaminergic system acutely and one day later. In the pr sent study, the authors sought to systematically det. the effects of **ibogaine** on the levels of dopamine (DA) and the dopamine **metabolites** 3,4-dihydroxyhenylacetic acid (DOPAC) and homovanillic acid (HVA) in tissue at several time points, between 1 h and 1 mo post-injection. One hour after **ibogaine** -administration (40 mg/kg i.p.), a 50% decrease in DA along with a 37-100% increase in HVA were obsd. in all 3 brain regions studied: striatum, nucleus accumbens and prefrontal cortex. Nineteen hours after **ibogaine**-administration, a decrease in DOPAC was seen in the nucleus accumbens and in the striatum. A week after administration of **ibogaine**, striatal DOPAC levels were still reduced. A month after **ibogaine** injection there, were no significant neurochem. changes in any region. The authors also investigated the effects of **ibogaine** pretreatment on

morphine-induced locomotor activity, which is thought to depend on DA release. Using photocell activity cages, it was found that **ibogaine** pretreatment decreased the stimulatory motor effects induced by a wide range of morphine doses (0.5-20 mg/kg i.p.) administered 19 h later; a similar effect was obsd. when morphine (5 mg/kg) was administered a week after **ibogaine** pretreatment. No significant changes in morphine-induced locomotion were seen a month after **ibogaine** pretreatment. The present findings indicate that **ibogaine** produces both acute and delayed effects on the tissue content of DA and its **metabolites**, and these changes coincide with a sustained depression of morphine-induced locomotor activity.

L28 ANSWER 10 OF 12 CA COPYRIGHT 1994 ACS DUPLICATE 8
AN 115:64663 CA
TI Interactions between ibogaine, a potential anti-addictive agent, and morphine: an in vivo microdialysis study
AU Maisonneuve, I. M.; Keller, R. W., Jr.; Glick, S. D.
CS Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA
SO Eur. J. Pharmacol. (1991), 199(1), 35-42
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB The indolalkylamine **ibogaine** may be effective in abolishing drug craving in heroin and cocaine addicts. In vivo microdialysis was used to det. the effects of **ibogaine** on brain extracellular levels of dopamine (DA) and its **metabolites** and the effects of **ibogaine** pretreatment on morphine stimulation of brain DA systems. **Ibogaine** (40 mg/kg i.p.) decreased extracellular DA levels in the striatum, increased them in the prefrontal cortex, and had no effects in the nucleus accumbens. At 19 h after **ibogaine** injection, DA levels were still decreased in the striatum and the **metabolite** levels were lower in all 3 regions. When injected 19 h prior to a morphine challenge (5 mg/kg i.p.), **ibogaine** (40 mg/kg, i.p.) prevented the rise in DA levels in all 3 regions normally obsd. after a morphine injection. A high dose of morphine (30 mg/kg i.p.) alone produced no increase in extracellular DA levels. It is unclear whether **ibogaine** antagonized or potentiated the effects of the lower dose of morphine. Regardless of the nature of this interaction, **ibogaine** effects brain DA systems for a period of time that exceeds its elimination from the body. During this tim **ibogaine** alters the responses of DA systems to morphine.

L28 ANSWER 11 OF 12 CA COPYRIGHT 1994 ACS
AN 110:87907 CA
TI Xenobiotic and endobiotic inhibitors of cytochrome P-450dbl function, the target of the debrisoquine/sparteine type polymorphism
AU Fonne-Pfister, Raymonde; Meyer, Urs A.
CS Biocent., Univ. Basel, Basel, CH-4056, Switz.
SO Biochem. Pharmacol. (1988), 37(20), 3829-35
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal

LA English
AB Five to 10% of Caucasians are poor metabolizers of debrisoquine, sparteine, bufuralol, and numerous other drugs. A deficiency in cytochrome P-450dbl (P-450dbl) function is the cause of this polymorphism of drug oxidn., which has autosomal recessive inheritance. In the present study, inhibition of bufuralol-1'-hydroxylase in human liver microsomes by drugs and other chems. was tested in a search for potential new substrates for this polymorphic enzyme. Of the 80 alkaloids and drugs tested, 25 were competitive inhibitors. In vitro competitive inhibition of bufuralol oxidn. by a substance indicates that this compd. is able to bind to the same enzymic site as bufuralol. This may mean that the competing drug also is metabolized by P-450dbl and that its metab. is subject to the same genetic variation as the oxidn. of bufuralol. However, some of these competitive inhibitors are not oxidized by P-450dbl. In this case, however, they may interfere with the in vivo phenotyping procedure by inhibiting the formation of **metabolites** of test drugs such as debrisoquine, sparteine, metoprolol, or dextromethorphan.

L28 ANSWER 12 OF 12 CA COPYRIGHT 1994 ACS
AN 103:42702 CA
TI High-performance liquid chromatographic analysis of basic drugs on silica columns using non-aqueous ionic eluents. II. Application of UV, fluorescence and electrochemical oxidation detection
AU Jane, I.; McKinnon, A.; Flanagan, R. J.
CS Metrop. Police Forensic Sci. Lab., London, SE1 7LP, UK
SO J. Chromatogr. (1985), 323(2), 191-225
CODEN: JOCRAM; ISSN: 0021-9673
DT Journal
LA English
AB Unmodified silica columns together with nonaq. ionic luents give stable yet flexible systems for the anal. of basic drugs by HPLC. Low-wavelength UV and fluorescence detection may be used, and fluorescence may be optimized by, post-column pH change or derivatization of some primary aliph. amines with o-phthaldialdehyde [643-79-8]. A novel feature is that electrochem. oxidn. can be used for the detection of most analytes and this detection mode is thus discussed in detail. Retention and relative response data (UV, 254 nm and electrochem., +1.2 V) were generated for 462 compds. using a 125-mm Spherisorb S5W silica column and methanolic NH4ClO4 (10 mM, pH 6.7) as eluent. This system can be used isocratically in qual. analyses and also for quant. work, when either the wavelength or the applied potential can be adjusted to optimize the response.

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FILE 'WPIDS' ENTERED AT 12:14:10 ON 14 OCT 94
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MOST RECENT DERWENT WEEK 9433 <199433/DW>
DERWENT WEEK FOR CHEMICAL CODING: 9426
DERWENT WEEK FOR POLYMER INDEXING: 9430

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=> d l25 1-8 std ab

L25 ANSWER 1 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 92-007193 [01] WPIDS
DNC C92-003067
TI Treatment of poly-drug dependency - with **ibogaine**, ibogamine or tabernanthine or their salts or deriv..
DC B02
IN LOTSOF, H S
PA (NDAI-N) NDA INT INC; (LOTS-I) LOTSOF H S
CYC 17
PI WO 9118609 A 911212 (9201)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: CA JP
US 5152994 A 921006 (9243) 4 pp A01N043-46
EP 511325 A1 921104 (9245) EN 15 pp A61K031-55
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
ADT US 5152994 A US 90-531100 900531; EP 511325 A1 EP 91-910992 910530, WO 91-US3781 910530
FDT EP 511325 A1 Based on WO 9118609
PRAI US 90-531100 900531
IC ICM A01N043-46; A61K031-55
ICS A61K009-08; A61K009-48
AB WO 9118609 A UPAB: 931006
Treating poly-drug dependency comprises internal admin. of **ibogaine**, ibogamine, tabernanthine, their therapeutically active cpds., their salts, or a mixt., to a subject dependent on heroin, cocaine, alcohol, caffeine, amphetamine, desoxyephedrine, nicotine, methadone or other opiate narcotics in one or mor combinations.
USE/ADVANTAGE - The method provides a high degree of success, with craving either totally interrupted or reversal or modification allowed, and is easy, convenient, rapid, acceptable to the addict population. There is absence of pain, discomfort, undesirable or persistent side effects. Effectiveness in the long term is good; a single treatment, or a series, interrupted drug desire for 1-18 months or longer.
0/0

L25 ANSWER 2 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 91-207487 [28] WPIDS
DNC C91-089966
TI Treating nicotine-tobacco dependency - by administering alkaloid of apocynaceae family on salt, e.g. **ibogaine** or ibogamine hydrochloride.
DC B02 D18
IN LOTSOF, H S

PA (NDAI-N) NDA INT INC
CYC 1
PI US 5026697 A 910625 (9128)*
ADT US 5026697 A US 90-530263 900530
PRAI US 90-530263 900530; US 90-580223 900910
IC A61K003-55
AB US 5026697 A UPAB: 930928
Method for treating nicotine/tobacco dependency comprises internal admin. of at least one Apolynaceae alkaloid (I) or its salt.
USE/ADVANTAGE - The method gives rapid interruption of physical and psychological withdrawal symptoms associated with nicotine or tobacco abuse. Dosage is 1-60 mg/kg orally or rectally as a single repeated admin. with successive administrations spaced at a plurality. @(4pp Dwg.No.0/0)

0 L25 ANSWER 3 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 89-300379 [41] WPIDS
DNN N89-229131 DNC C89-132881
TI Alcohol dependency and abuse treatment - comprises administering **ibogaine** and/or its non-toxic salts.
DC B02 P34
IN LOTSOF, H S
PA (NDAI-N) NDA INT INC
CYC 1
PI US 4857523 A 890815 (8941)* 3 pp
ADT US 4857523 A US 88-221030 880718
PRAI US 88-221030 880718
IC A61U031-55
AB US 4857523 A UPAB: 930923
Treating alcohol dependency and abuse comprises internally administering a dosage of 4-25 mg/kg of **ibogaine** and/or its therapeutically active cpd.
The dosage is administered orally and the compsn. contains **ibogaine** and/or its hydro chloride or hydrobromide in a dosage of 400-1000 mg. The dosage is pref. in capsule, tablet, pill, powder or soln. form and is admixed with binders or fillers. A plurality of dosages are administered, intervals of a number of days intervening between successive dosages. A single treatment is effective for about 6 months.
USE/ADVANTAGE - The method is partic. for lessening the physiological and psychological aspects of alcohol habituation. It has a high degree of success, with the absence of pain and discomfort accompanying earlier treatments and is easy and convenient to use. There are no undesirable or persistent side effects and the invention is non-addicting and in a series of treatments will remove any potential for its own abuse.
0/0

/L25 ANSWER 4 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 86-137162 [21] WPIDS
DNC C86-058803
TI Interruption of cocaine and amphetamine abuse syndrome - using **ibogaine** or salts.
DC B02

PA (LOTS-I) LOTSOF H S
CYC 1
PI US 4587243 A 860506 (8621)* 4 pp
ADT US 4587243 A US 85-754836 850715
PRAI US 85-754836 850715
IC A61K031-55
AB US 4587243 A UPAB: 930922
Method of treating cocaine and/or amphetamine obuse comprises admin. of **ibogaine** (I) and/or its therapeutically active cpd(s)., pref. a non-toxic salt, esp. HCl or HBr salt. Dose is pref. 6-19 mg/kg, pref. p.o., in units of 400-1000 mg.. Pref. admin. is spaced with a no. of days between successive doses.
ADVANTAGE - (I) disrupts the cocaine/amphetamine habituation syndrome, is not a euphoriant hallucinogen, and does not leave the subject open to swells of emotion. Treatment is effective and undesirable or persistent side-effects are absent.
0/0

L25 ANSWER 5 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 85-055920 [09] WPIDS
DNC C85-024345
TI Long lasting treatment of heroin addiction - by oral admin. of **ibogaine** (hydrochloride or hydrobromide salt).
DC B02
PA (LOTS-I) LOTSOF H S
CYC 27
PI US 4499096 A 850212 (8509)* 4 pp
WO 8502115 A 850523 (8522) EN
RW: AT BE CF CG CH CM DE GA GB LU MR NL SE SN TD TG
W: AU DK FI JP
NO 8404573 A 850610 (8530)
AU 8436744 A 850603 (8535)
EP 163697 A 851211 (8550) EN
R: CH DE FR GB LI NL
DK 8503164 A 850711 (8713)
CA 1237986 A 880614 (8828)
EP 163697 B 900523 (9021)
R: CH DE FR GB LI NL
IL 73585 A 900429 (9026)
DE 3482305 G 900628 (9027)
IT 1178249 B 870909 (9035)
ADT US 4499096 A US 83-553138 831118; WO 8502115 A WO 84-US1851 841113
PRAI US 83-553138 831118
IC A61K031-43; A61K043-00; C07D471-18; C07D487-00
AB US 4499096 A UPAB: 930925
Heroin addiction may be treated by admin. of **ibogaine** (I) (or its deriv.) at a dosage of 6-19 mg/kg. Oral treatment using (I), its hydrochloride or hydrobromide, is also claimed.
ADVANTAGE - The method avoids the great pain and discomfort associated with prior art treatments, and does not show persistent side effects. A high degree of success in alleviating addiction is shown as there is rapid interruption of physiological and psychological withdrawal and the elimination of the addicts desire to use heroin for about six months. (I) itself is non-addicting, and

in a series of treatments will remove its own potential for abuse.
0/0

L25 ANSWER 6 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 73-10754U [08] WPIDS
TI 10-methoxyibogamine formyl and acetyl derivs - - as analgetic and anti-inflammatory agents.
DC B02
PA (AMCY) AMERICAN CYANAMID CO
CYC 1
PI US 3715361 A (7308)*
PRAI US 71-187895 711008
IC C07D043-38
AB US 3715361 A UPAB: 930831
New ibogamine derivs. of formula: (where (I) R = CHO, R1 = R" = H, (II) R1 = CHO, R = R" = H, (III) R1 = CHO, R = H, R" = CH3 and (IV) R1 = R" = COCH3, R = H) and their non-toxic acid addition salts are useful as analgetic and anti-inflammatory agents. I, II and III are prepared from 10-methoxyibogamine (**ibogaine**) by formylation using the Vilsmeier-Hack reaction or a modification of it and (IV) is prepared by acetylating **ibogaine** with acetic acid, acetic anhydride and BF3.

L25 ANSWER 7 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-39590F [00] WPIDS
TI Amphetamine mixed with tabernanthe iboga alkaloids.
DC B00
PA (BOCH) BOCHER DPM
CYC 5
PI BE 726760 A (6800)*
DE 1902227 A (6801)
FR 7131 M (7046)
GB 1256914 A (7149)
CA 939266 A (7402)
PRAI FR 68-138081 680131
AB BE 726760 A UPAB: 930831
The association of amphetamine or one of its derivs. with an alkaloid extract of Tabernanthe iboga, a total extract of this plant, or pure **ibogaine**.
Useful in psychotherapy. The alkaloids clear the thought of the patient, giving him an extra-lucid vision of hims lf, and assisting him to remember his early life before the age of 4. The amphetamine brings a stimulation of the emotions to balance the intellectual stimulation. The use of this treatment may shorten the course of treatment considerably.

L25 ANSWER 8 OF 8 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-00948F [00] WPIDS
TI Analgesic compns.
DC B00
PA (CIBA) CIBA LTD
CYC 1
PI GB 841697 A (6800)*
AB GB 841697 A UPAB: 930831

Analgesics of the morphine series such as morphine, codeine, codeine derivatives, dihydro-morphinone, methyl-dihydromorphinone, pantopon, ethylmorphine, -ketobemidone, meperidine, dihydrocodeinone, dihydromorphine, dihydro-desoxymorphine-D, dihyrodesoxycodeine-D, dl-3-methoxy-N-methyl-morphinan and dl-3-hydroxy -N-methylmorphinan are potentiated with **ibogaine** or tavern-xanthine. The latter are indole alkaloids isolated from the plant Tabernanthe Iboga. The weight ratio of alkaloid: narcotic is 0.5-20:1

=>
=>
=>
=> fil reg
FILE 'REGISTRY' ENTERED AT 12:17:48 ON 14 OCT 94
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COPYRIGHT (C) 1994 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 8 OCT 94 HIGHEST RN 158188-97-7
DICTIONARY FILE UPDATES: 13 OCT 94 HIGHEST RN 158188-97-7

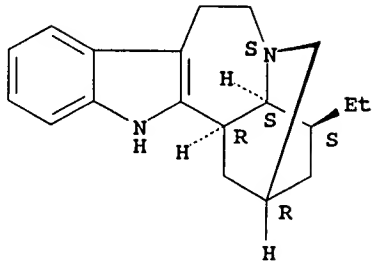
TSCA INFORMATION NOW CURRENT THROUGH MAY 1994

Please note that search-term pricing does apply when conducting SmartSELECT searches.

=> d ide can l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1994 ACS
RN 481-87-8 REGISTRY
CN Ibogamine (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine deriv. (9CI)
OTHER NAMES:
CN (-)-Ibogamine
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, 7-ethyl-6,6a,7,8,9,10,12,13-octahydro-, [6R-(6.alpha.,6a.beta.,7.beta.,9.alpha.)]-
CN **Ibogamin**
CN [6R-(6.alpha.,6a.beta.,7.beta.,9.alpha.)]-7-Ethyl-6,6a,7,8,9,10,12,13-octahydro-6,9-methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole
FS STEREOSEARCH
MF C19 H24 N2
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CHEMINFORMRX, DDR, DRUGR, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, NAPRALERT, SPECINFO, TOXLINE, TOXLIT
(*Fil contains numerically searchable property data)
DES 4:.IBOGAMINE

Absolute stereochemistry.



57 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
30 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 116:143736

REFERENCE 2: P 116:100980

REFERENCE 3: 116:55592

REFERENCE 4: 116:37986

REFERENCE 5: P 116:17031

REFERENCE 6: 112:155225

REFERENCE 7: 110:189357

REFERENCE 8: 110:154646

REFERENCE 9: 109:122005

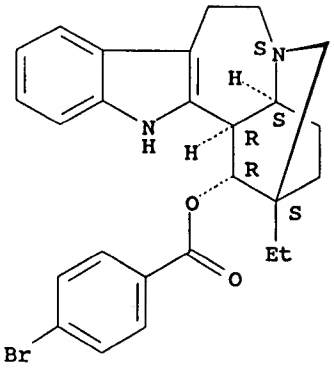
REFERENCE 10: 108:204858

=>
=> d ide can l3 1-8

L3 ANSWER 1 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN **88660-09-7** REGISTRY
CN 20,21-Dinoribogamin-1-ol, 2-ethyl-, 4-bromobenzoate (ester), (1.alpha.)-(.+-.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, 20,21-dinoribogamin-1-ol deriv. (9CI)
OTHER NAMES:
CN **(.+-.)-16-Hydroxy-allo-ibogamine p-bromobenz ate**
FS STEREOSEARCH

MF C26 H27 Br N2 O2
LC STN Files: CA
DES 3:(+-)4:1A.IBOGAMINE

Racemate. One enantiomer shown.

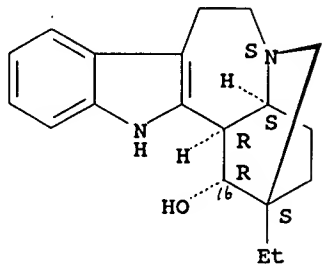


1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 100:64969

L3 ANSWER 2 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN **88660-07-5** REGISTRY
CN 20,21-Dinoribogamin-1-ol, 2-ethyl-, (1.alpha.)-(.+-.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, 20,21-dinoribogamin-1-ol deriv. (9CI)
OTHER NAMES:
CN **(.+-.)-16-Hydroxy-allo-ibogamine**
FS STEREOSEARCH
MF C19 H24 N2 O
LC STN Files: CA
DES 3:(+-)4:1A.IBOGAMINE

Racemate. One enantiomer shown.

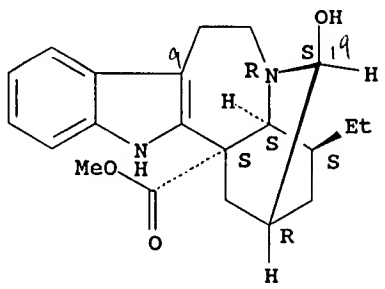


1 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 100:64969

L3 ANSWER 3 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN 77123-15-0 REGISTRY
CN **Ibogamine-18-carboxylic acid, 19-hydroxy-, methyl ester, (19S)-**
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)
OTHER NAMES:
CN (19S)-Hydroxycoronaridine
CN (3S)-Hydroxycoronaridine
FS STEREOSEARCH
MF C21 H26 N2 O3
LC STN Files: BEILSTEIN*, CA
(*File contains numerically searchable property data)
DES 4:19S.IBOGAMINE

Absolute stereochemistry.



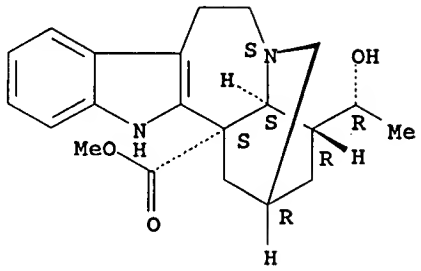
2 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 103:160748

REFERENCE 2: 94:157129

L3 ANSWER 4 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN **57511-56-5** REGISTRY
CN **Ibogamine-18-carboxylic acid, 20-hydroxy-, methyl ester, (4.alpha.,20R)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)
OTHER NAMES:
CN (-)-19-Epiheyneanine
CN 19-Epiheyneanine
CN 19R-Heyneanine
CN 20-Epiheyneanine
CN Epiheyneanin
CN Epiheyneanine
FS STEREOSEARCH
MF C21 H26 N2 O3
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, NAPRALERT, TOXLIT
(*File contains numerically searchable property data)
DES 4:4A,20R.IBOGAMINE

Absolute stereochemistry.



22 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 118:124850

REFERENCE 2: 114:58868

REFERENCE 3: 111:17218

REFERENCE 4: 108:167739

REFERENCE 5: 107:95165

REFERENCE 6: 107:93506

REFERENCE 7: 107:46385

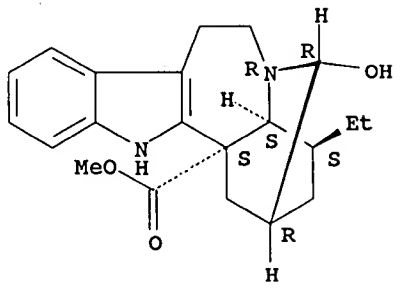
REFERENCE 8: 104:213084

REFERENCE 9: 103:211119

REFERENCE 10: 102:201148

L3 ANSWER 5 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN 53508-36-4 REGISTRY
CN **Ibogamine-18-carboxylic acid, 19-hydroxy-, methyl ester, (19R)-**
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)
OTHER NAMES:
CN (-)-Eglandine
CN (19R)-Hydroxycoronaridine
CN (3R)-Hydroxycoronaridine
CN Eglandine
FS STEREOSEARCH
DR **77171-01-8**
MF C21 H26 N2 O3
LC STN Files: BEILSTEIN*, CA, NAPRALERT
(*File contains numerically searchable property data)
DES 4:19R.IBOGAMINE

Absolute stereochemistry.



7 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 114:58868

REFERENCE 2: 103:160748

REFERENCE 3: 95:147100

REFERENCE 4: 83:111127

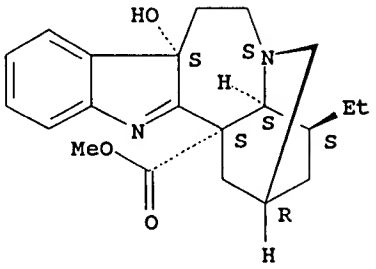
REFERENCE 5: P 83:97685

REFERENCE 6: 81:120844

REFERENCE 7: P 81:91779

L3 ANSWER 6 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN **16671-16-2** REGISTRY
CN **Ibogamine-18-carboxylic acid, 16,17-didehydro-9,17-dihydro-9-hydroxy-, methyl ester, (9.alpha.)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-8H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)
CN Coronaridine hydroxyindolenine (8CI)
OTHER NAMES:
CN Hydroxyindolenine-coronaridine
FS STEREOSEARCH
MF C21 H26 N2 O3
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, NAPRALERT
(*File contains numerically searchable property data)
DES 4:9A.IBOGAMINE

Absolute stereochemistry.



16 REFERENCES IN FILE CA (1967 TO DATE)

REFERENCE 1: 120:212597

REFERENCE 2: 116:55592

REFERENCE 3: 114:58868

REFERENCE 4: 109:107714

REFERENCE 5: 102:163683

REFERENCE 6: 102:146159

REFERENCE 7: 102:128845

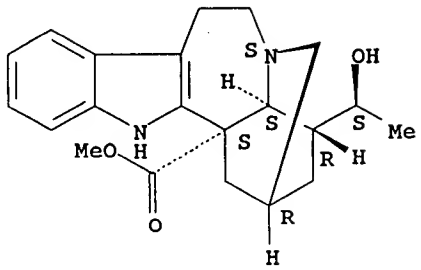
REFERENCE 8: 100:103692

REFERENCE 9: 97:52527

REFERENCE 10: 95:147100

L3 ANSWER 7 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN **4865-78-5** REGISTRY
CN **Ibogamine-18-carboxylic acid, 20-hydroxy-, methyl ester, (4.alpha.,20S)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-5H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)
CN Heyneanine (7CI)
OTHER NAMES:
CN (-)-Heyneanine
CN Heyneanin
FS STEREOSEARCH
DR 100657-71-4
MF C21 H26 N2 O3
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, NAPRALERT, SPECINFO, TOXLIT
(*File contains numerically searchable property data)
DES 4:4A,20S.IBOGAMINE

Absolute stereochemistry.



30 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 116:55592

REFERENCE 2: 114:58868

REFERENCE 3: 111:17218

REFERENCE 4: 110:189357

REFERENCE 5: 110:111819

REFERENCE 6: 109:107714

REFERENCE 7: 107:83746

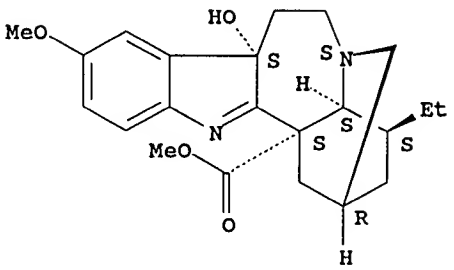
REFERENCE 8: 106:116489

REFERENCE 9: 104:65956

REFERENCE 10: 102:163683

L3 ANSWER 8 OF 8 REGISTRY COPYRIGHT 1994 ACS
RN 3464-63-9 REGISTRY
CN **Ibogamine-18-carboxylic acid, 16,17-didehydro-9,17-dihydr -9-hydroxy-12-methoxy-, methyl ester, (9.alpha.)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6,9-Methano-8H-pyrido[1',2':1,2]azepino[4,5-b]indole-6(6aH)-carboxylic acid, 7-ethyl-7,9,10,12,13,13a-hexahydro-13a-hydroxy-2-methoxy-, methyl ester (7CI)
CN 6,9-Methano-8H-pyrido[1',2':1,2]azepino[4,5-b]indole, ibogamine-18-carboxylic acid deriv. (9CI)
CN 9H-Voacangine, 9-hydroxy- (8CI)
OTHER NAMES:
CN 7-Hydroxy-1-dehydrovoacangine
CN Voacangine 7-hydroxyindolenine
CN Voacangine hydroxyindolenine
FS STEREOSEARCH
DR 19779-79-4
MF C22 H28 N2 O4
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, NAPRALERT
(*File contains numerically searchable property data)
DES 4:9A.IBOGAMINE

Absolute stereochemistry.



```
L49          18 S IBOGAMIN# OR HYDROXYIBOGAMIN#
L50          18 S L48 OR L49
L51           1 S D15.160./CT AND L50
L52           0 S L50 AND ADDICTION+NT/CT
L53           2 S L50 AND INTOXICATION+NT/CT
L54           1 S ALLOIBOGAINE OR 9 HYDROXY 9 H IBOGAMINE
L55           3 S L51 OR L53 OR L54
L56           0 S L50 AND (ALCOHOL ABUSE+NT/CT OR DRUG ABUSE+NT/CT)

     FILE 'WPIDS' ENTERED AT 12:33:37 ON 14 OCT 94
L57           7 S ?IBOGAMIN?
L58           4 S L57 NOT L25

=> fil hca
FILE 'HCA' ENTERED AT 12:34:35 ON 14 OCT 94
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FILE COVERS 1967 - 1 Oct 1994 (941001/ED)  VOL 121 ISS 14

THE BASIC INDEX NOW INCLUDES ABSTRACT TEXT.  SEE NEWS FOR DETAILS.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCA' FILE

=> d 138 1-6 bib ab hitrn

L38  ANSWER 1 OF 6  CA  COPYRIGHT 1994 ACS
AN   116:143736  CA
TI   Mechanisms of action of ibogaine and harmaline congeners based on
     radioligand binding studies
AU   Deecher, Darlene C.; Teitler, Milton; Soderlund, David M.; Bornmann,
     William G.; Kuehne, Martin; Glick, Stanley D.
CS   Dep. Pharmacol. Toxicol., Albany Med. Coll., Albany, NY, 12208, USA
SO   Brain Res. (1992), 571(2), 242-7
     CODEN: BRREAP; ISSN: 0006-8993
DT   Journal
LA   English
AB   Assays using radioligands were used to assess the actions of
     ibogaine and harmaline on various receptor types.  Ibogaine
     congeners showed affinity for opiate receptors whereas harmaline and
     harmine did not.  The Ki for coronaridine was 2.0 .mu.M at
     .mu.-opiate receptors.  The Kis for coronaridine and tabernanthine
     at the .delta.-opiate receptors were 8.1 and 3.1 .mu.M, resp.
     Ibogaine, ibogamine, coronaridine, and tabernanthine had
     Ki values of 2.08, 2.6, 4.3 and 0.15 .mu.M, resp., for
     .kappa.-opiate receptors.  Long-lasting, dose-dependent behavioral
     effects of ibogaine have been reported.  The possibility that these
     effects were due to irreversible binding properties of ibogaine at
     .kappa.-receptors was considered; however, radioligand wash expts.
     showed a rapid recovery of radioligand binding after one wash.  A
     voltage-dependent sodium channel radioligand demonstrated Ki values
     in the .mu.M range for all drugs tested.  Using radioligand binding
     assays and/or 36Cl- uptake studies, no interaction of ibogaine or
     harmaline with the GABA receptor-ionophore was found.  The
     .kappa.-activity of ibogaine (or an active metabolite) may be
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responsible for its putative anti-addictive properties whereas the tremorigenic properties of ibogaine and harmaline may be due to their effects on sodium channels.

IT **481-87-8, Ibogamine**
(receptor affinity for, mechanism of action in relation to)

L38 ANSWER 2 OF 6 CA COPYRIGHT 1994 ACS
AN 116:100980 CA
TI A rapid method for interrupting or attenuating poly-drug dependency syndromes
IN Lotsof, Howard S.
PA NDA International, Inc., USA
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
PI WO 9118609 A1 911212
DS W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
AI WO 91-US3781 910530
PRAI US 90-531100 900531
DT Patent
LA English
AB The administration of ibogaine, **ibogamine**, tabernanthine, or their nontoxic salts interrupts the physiol. and psychol. aspects of poly-drug dependency to heroin, cocaine, alc., nicotine, caffeine, amphetamine, desoxyephedrine, or methadone in combinations thereof. A single treatment or series of treatments may be effective for 1-18 mo or longer. A patient addicted to alc., cocaine, and heroin was treated with ibogaine; a single dose of ibogaine at 15 mg/kg body wt. completely interrupted heroin and cocaine use and diminished alc. use by 50-80 % on a daily basis.

IT **481-87-8, Ibogamine 481-87-8D, Ibogamine**, salts with tannic acid
(**drug dependence** treatment with)

L38 ANSWER 3 OF 6 CA COPYRIGHT 1994 ACS
AN 116:17031 CA
TI Rapid method for interrupting or attenuating the nicotine/tobacco dependency syndrome using Apocyanaceae alkaloids
IN Lotsof, Howard S.
PA NDA International, Inc., USA
SO U.S., 4 pp.
CODEN: USXXAM
PI US 5026697 A 910625
AI US 90-530263 900530
DT Patent
LA English
AB The administration to a nicotine or tobacco addict of ibogaine, **ibogamine**, or tabernanthine or nontoxic salts of these alkaloids of the family Apocyanaceae interrupts the physiol. and psychol. aspects of nicotine or tobacco dependency. A single treatment or series of treatments may be effective for .gtoreq.1-18 mo. Dose ranges are 1-60 mg/kg for oral, rectal infusion, or suppository administration of the above alkaloids. Thus, a subject who was smoking .gtoreq.2 packs of filter cigarets per day was

administered a single dose of 15 mg ibogaine/kg. The subject suffered no nicotine withdrawal and has not smoked cigarets for >24 mo., at which time tracking ceased.

IT **481-87-8, Ibogamine 481-87-8D,**
Ibogamine, tannic acid salts
(for tobacco/nicotine dependency treatment)

L38 ANSWER 4 OF 6 CA COPYRIGHT 1994 ACS
AN 109:122005 CA
TI Non-amphetaminic central stimulation by alkaloids from the ibogane and vobasine series
AU Bert, Maryse; Marcy, Rene; Quermonne, Marie Anne; Cotelle, Michel; Koch, Michel
CS Dep. Pharmacogn., UER Sci. Pharm., Caen, F-14000, Fr.
SO Planta Med. (1988), 54(3), 191-2
CODEN: PLMEAA; ISSN: 0032-0943
DT Journal
LA English
AB Ibogane alkaloids I (R1 and R2 = H, OMe; R3 = H, CH2OH, CO2Me, CH2OAc, or vobasinyl) had a very high arousal activity in mice. Similarly, a CNS-stimulating activity was demonstrated for vobasine alkaloids II (R = H; R1 = OH, S(CH2)2NH2; RR1 = O; R2 = H, Me). The influence of certain substituents was shown; methoxy substitution increased the activity, while it was lowered by methoxycarbonyl substitution.

IT **481-87-8D, Ibogamine**, derivs.
(central **nervous** system-**stimulant** activity of, structure in relation to)

L38 ANSWER 5 OF 6 CA COPYRIGHT 1994 ACS
AN 75:6166 CA
TI Iboga alkaloid derivatives as central **nervous** system **stimulants**
IN Sallay, Stephen I.
PA am homme
SO U.S., 7 pp.
CODEN: USXXAM
PI US 3557126 710119
AI US 690814
DT Patent
LA English
AB A synthesis of **ibogamine** (I) is described via II-XV in which the indole ring closure of cis-9-ethyloctahydro-1,7-methano-1H-benzazepin-5(4H)-one as the last step provides versatility in the prepn. of Iboga alkaloids.

L38 ANSWER 6 OF 6 CA COPYRIGHT 1994 ACS
AN 73:131198 CA
TI Central-**nervous**-system **stimulant** derivatives of Iboga alkaloids and Iboga intermediates
IN Sallay, Stephen I.
PA American Home Products Corp.
SO U.S., 8 pp.
CODEN: USXXAM

PI US 3516989 700623
AI US 671002
DT Patent
LA English
AB trans-1,3-Hexadiene (194 g) in 2500 ml benzene was refluxed for 2 hr with 286 g p-quinone to give d,l-cis-5.beta.-ethyl-4a,5,8,8a-tetrahydro-1,4-naphthoquinone (I), m. 46-8.degree.. I was reduced with HOAc and Zn dust to give d,l-cis-5.beta.-ethyl-2,3,4a,5,8,8a-hexahydro-1,4-naphthoquinone (II), m. 71-3.degree.. II (247 g) in 500 ml CH2Cl2 and 600 ml HOAc was treated with 88 g HOCH2CH2OH in 360 ml HOAc and 186 g BF3.Et2O in 250 ml HOAc to give d,l-cis-5'.beta.-ethyl-2',3',4'a,5',8',8'a-hexahydrospiro[1,3-dioxolane- 2,1'(4'H)-naphthalen]-4'-one (III), b0.01 104.degree.. III was heated to 60.degree. with 1 mole equiv. of hydroxylamine acetate in MeOH (from 102 g NH2OH.HCl and 118 g NaOAc) to give 260 g III oxime (IV), m. 125-6.degree.. IV (100 g) in pyridine was treated at 75.degree. with 76 g p-MeC6H4SO2Cl to give 83.8 g d,l-cis-9.beta.-ethyl-3,4,5a,6,9,9a-hexahydrospiro[5H-1-benzazepino-5,2'- (1,3)-dioxolane]-2(1H)-one (V), m. 144-5.degree.. V (50 g) was oxidized with 0.2 mole m-ClC6H4CO2OH to give d,l-cis-7.alpha.,8.alpha.-epoxy-9.beta.-ethyl-3,4,5a,6,7,8,9,9a-octahydrospiro[5H-1- benzazepino-5,2'-(1,3)-dioxolan]-2(1H)-one (VI), m. 170-1.degree.. Redn. with LiAlH4 converted VI to d,l-cis-9.beta.-ethyl-3,4,5a,6,7,8,9,9a-octahydro-7a-hydroxyspiro[5H-1- benzazepino-5,2'-(1,3)-dioxolan]-2(1H)-one (VII), m. 180-1.5.degree.. VII (9 g) in pyridine was oxidized with a CrO3-pyridine complex (from 8.0 g CrO3 and 120 ml pyridine, below 25.degree.) to give 7.6 g d,l-cis-9.beta.-ethyl-3,4,5a,6,9,9a-hexahydrospiro[5H-1-benzazepino-5,2'- (1,3)-dioxolane]-2,7(1H)-dione (VIII), m. 220.degree.. VIII (2.6 g) in 100 ml Me2SO was treated with triphenylphosphonium methylide (prepd. dimsylsodium from Me2SO and PH3PMeBr) and the mixt. heated to 30-40.degree. for a few hr to give 2.14 g d,l-cis-9-ethyloctahydro-7-methylenespiro[5H-1-benzazepine-5,2'-(1,3)- dioxolane]-2(1H)-one (IX), m. 196-7.degree.. IX (2.3 g) was treated with 1 mole equiv. diborane at 10.degree. and the mixt. kept overnight. The mixt. was then treated with 4 ml 10% NaOH and 2 ml 50% H2O2 and excess H2O2 decompd. with Pd-C to give d,l-cis-9-ethyloctahydro-7-hydroxymethylspiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-2(1H)-one (X). This lactam in THF was reduced with LiAlH4 to give d,l-cis-9-ethyldecahydrospiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane-7- methanol (XI) as a gum. XI (11.6 g) was treated with N LiOH and 12 g carbobenzoxy chloride at 10.degree. to form d,l-cis-9-ethyloctahydro-7-hydroxymethylspiro[5H-1-benzazepine-5,2'-(1,3)-dioxolane]-1(2H)-carboxylic acid benzyl ester (XII). XII was treated with p-MeC6H4SO2Cl to form the tosyl ester of XII, which was treated with HOAc and HBr to give the hydrobromide of XII. This compd. (1 g) in NaOH was extd. with CH2Cl2, the base refluxed for 10 hr in isoamyl alc., and the resulting compd. treated with HBr gas to give d,l-cis-9-ethyloctahydro-1,7-methano-1H-1-benzazepin-5(4H)-one-HBr. Treatment of this salt with H2SO4 followed by 0.3 ml PhNNH2 gave **ibogamine**.

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=> d l55 1-3 bib ab

L55 ANSWER 1 OF 3 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN 94278996 EMBASE
TI Effects of iboga alkaloids on morphine and cocaine self-administration in rats: Relationship to tremorigenic effects and to effects on dopamine release in nucleus accumbens and striatum.
AU Glick S.D.; Kuehne M.E.; Raucci J.; Wilson T.E.; Larson D.; Keller R.W. Jr.; Carlson J.N.
CS Dept. Pharmacology Toxicol. (A-136), Albany Med. Coll. Capital Districts, Ctr. Drug Abuse Res. and Treatment, Albany, NY 12208, United States
SO BRAIN RES., (1994) 657/1-2 (14-22).
ISSN: 0006-8993 CODEN: BRREAP
CY Netherlands
DT Journal
FS 030 Pharmacology
040 Drug Dependence, Alcohol Abuse and Alcoholism
037 Drug Literature Index
LA English
SL English
AB Ibogaine, a naturally occurring alkaloid, has been claimed to be effective in treating addiction to opioid and stimulant drugs and has been reported to decrease morphine and cocaine self-administrationin rats. The present study sought to determine if other iboga alkaloids, as well as the chemically related harmala alkaloid harmaline, would also reduce the intravenous self-administration of morphine and cocaine in rats. Because both ibogaine and harmaline induce tremors, an effect that may be causally related to neurotoxicity in the cerebellar vermis, the temorigenic activities of the other iboga alkaloids wer assessed. Lastly, in view of the involvement of the dopaminergic mesolimbic system in the actions of drugs of abuse, the effects of some of the iboga alkaloids on extracellular levels of dopamine and its metabolites in the nucleus accumbens and striatum were determined. All of the tested alkaloids (i.e., ibogaine, tabernanthine, R- and S-coronaridine, R- and S-**ibogamine**, desethylcoronaridine, and harmaline) dose-dependently (2.5-80 mg/kg) decreased morphine and cocaine intake in the hour after treatment; decreases in morphine and cocaine intake intake were also apparent the day after administration of some but not all of these alkaloids (i.e., ibogaine, tabernanthine, desethylcoronaridine, and the R-isomers of coronaridine and **ibogamine**). In some rats, there were persistent decreases in morphine or cocaine intake for several bays after a single injection or after two or three weekly injections of one or another of these alkaloids; R-**ibogamine** produced such effects more consistently than any of the other alkaloids. At

the doses used to assess effects on drug self-administration, ibogaine, tabernanthine, desethylcoronaridine and harmalin all induced tremors for at least 2-3 h; both enantiomers of both coronaridine and **ibogamine** induced very weak or no tremors. Using in vivo microdialysis, the effects of the R- and S-enantiomers of coronaridine and **ibogamine** on extracellular dopamine levels in the nucleus accumbens and striatum were compared. The R-enantiomers decreased dopamine levels in both brain regions whereas the S-enantiomers produced no significant changes in dopamine levels in either region. The results of this study indicate that the 'anti-addictive' and tremorigenic effects of the iboga alkaloids can be dissociated and that long-term effects of these alkaloids on drug self-administration appear to be r lated to initial decreases in dopaminergic activity in specific brain areas.

L55 ANSWER 2 OF 3 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN 84016445 EMBASE
TI Tertiary indole alkaloids of Tabernaemontana dichotoma seeds.
AU Perera P.; Sandberg F.; Van Beek T.A.; Verpoorte R.
CS Dep. Pharmacogn., Biomed. Cent., Univ. Uppsala, S-75123 Uppsala, Sweden
SO PLANTA MED., (1983) 49/1 (28-31).
CODEN: PLMEAA
CY Germany, Federal Republic of
LA English

L55 ANSWER 3 OF 3 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN 78308335 EMBASE
TI [Alkaloids of Tabernanthe iboga].
LES ALCALOIDES DE L'IBOGA (TABERNANTHE IBOGA H.Bn.).
AU Gaignault J.C.; Delourme-Houde J.
CS Cent. Rech. Roussel Uclaf Romainville, Paris, France
SO FITOTERAPIA, (1977) 48/6 (243-265).
CODEN: FTRPAE
CY Italy
LA French

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L58 ANSWER 1 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 71-26418S [15] WPIDS
TI Cis-9-alkyloctahydro-1,7-methano-1h-1-benz- - azepin-5-(4h)-ones, intermediates for iboga.
DC B02
PA (AMHP) AMERICAN HOME PROD CORP
CYC 1
PI US 3574220 A (7115)*
PRAI US 67-671966 671002; US 69-870997 690814
IC C07D039-00
AN 71-26418S [15] WPIDS
AB US 3574220 A UPAB: 930831
Cis-9-alkyloctahydro-1,7-methano-1H-1-bezazepin-5-(4H)-ones, intermediates for iboga alkaloids. Cpds. of formula:- (where R1 is 1-6C alkyl), are converted to iboga alkaloids, which ar CNS stimulants, by condensation with phenylhydrazine or ring-substituted derivs. thereof. The cpds. are prepd. by cyclization of cis-9-alkyl-decahydro-7-tosyloxymethyl-5H-benzazepin-5-ones. Thus dl-cis-9-ethyldecahydro-7-tosyloxymethyl-5H-benzazepin-5-on is refluxed in iso-amyl alcohol to give, after gasification, dl-cis-9-ethyloctahydro-1,7-methano-1H-1-benzazepin-5(4H)-one, which, on condensation with phenylhydrazine, gives **ibogamine**
.

L58 ANSWER 2 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-35100F [00] WPIDS
TI (A) Cpds. (I) R - H or lower alkyl (B) Method for isoquinuclidine alkaloids (X). Anti-tumour, anti-protozoals, analeptics, analgesics, and ant.
DC B02
PA (SHIO) SHIONOGI & CO LTD
CYC 8
PI NL 6807826 A 681203 (6800)*
FR 1572766 A (6801)
JP 45039270 B (7049)
JP 46004180 B (7105)
GB 1236488 A (7124)
CH 510669 A (7141)
CH 511233 A (7141)
US 3639408 A (7210)
CH 518940 A (7220)
CA 913103 A (7245)
CA 913104 A (7245)
US 3716528 A (7309)
DE 1770561 A 711104 (8523)
PRAI JP 67-35647 670603; JP 68-7620 680207
IC C07D039-06
AN 66-35100F [00] WPIDS
AB NL 6807826 A UPAB: 930831
(A) Cpds.
(I) R = H or lower alkyl
(B) Method for isoquinuclidine alkaloids (X).
Anti-tumour, anti-protozoals, analeptics, analgesics, and

antivirals.
(a)
(b) R' and R2 = H or lower alkyl
X = an organic acid residue, e.g. p-Me.C6H4SO2
Y = lower alkyl
Z and Z' = H, lower alkyl, lower Oalkyl or halogen.
desethylibogamine, m.p.184-6.

✓L58 ANSWER 3 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-02183F [00] WPIDS
TI Ester alkaloids of indole series.
DC B00
PA (GEIG) GEIGY AG
CYC 3
PI DE 1132561 A (6800)*
JP 38006478 B (6801)
NL 249100 B (6801)
AN 66-02183F [00] WPIDS
AB DE 1132561 A UPAB: 930831
Ester alkaloids of indole series wherein the benzene ring may be substd. by methoxy and R is lower alkyl) or the indolenine are decarbalkoxylated by heating with a base R1 - NH2 (wher R1 is amino alkylamino, aralkylamino, cycloalkylamino, alkyl, in the presence of a solvent and opt. in N2 atmosphere. Suitabl starting materials are voacangin, isovoacangin, voacristin, and 12:13-dimethoxy-coronaridin, and the base may be hydrazine or hydrazine hydrate. The 12:13-dimethoxy-**ibogamin**. obtd. from
12:13-dimethoxy-coronaridin is new cpd. which potentiates analgetics, such as morphine and aminopyrin and it also shows analgetic activity.

✓L58 ANSWER 4 OF 4 COPYRIGHT 1994 DERWENT INFORMATION LTD
AN 66-02181F [00] WPIDS
TI 12 13-**dimethoxyibogamine**.
DC B00
PA (GEIG) GEIGY A-G JR
CYC 4
PI DE 1134082 A (6800)*
CH 372291 A (6801)
GB 924042 A (6801)
NL 249096 B (6801)
AN 66-02181F [00] WPIDS
AB DE 1134082 A UPAB: 930831
New 12:13-dimethoxy-**ibogamine** is an isoquinuclidine alkaloid
effective against the effect of reserpine in mice. It is prepared by treating 12:13-dimethoxycoronaridine (extracted from the stem bark of Conopharyngia durissima Staff) with a soln. of an alkali hydroxide in an alcohol and decarboxylating the intermediate product obtained by heating in an acid medium. In an Example, 2 pt. 12:13-dimethoxycoronaridine and 50 pt. 20% methanolic KOH are heated under reflux for 6 hrs., pref. under N2. The soln. is then cooled, methanol removed under vacuum, the

residue dissolved in water, acidified with HCl (pH < 2), heated for 2 hrs. at 80-90 deg.C, cooled, made alkaline with NH3, the pptd. base filtered, and recrystallised from methanol to give 0.85 pt. of product, m.pt. 136 deg.C. On recrystallisation from ether-petroleum ether a crystalline 12:13-dimethoxy-**ibogamine** of
m.pt. 146 deg.C is obtained.